

# Allergic Rhinitis in Relation to Gut Microbiota Composition among School-Aged Patients

Samir Sourour<sup>1</sup>, Mahmoud Diab<sup>1</sup>, Rania M. Amer<sup>2</sup>, Tarek Abdelmouty<sup>1</sup>,  
Gehan A. Elshenawy<sup>2</sup>, Saeid Abdelmonaem<sup>1</sup>

<sup>1</sup>Department of Otorhinolaryngology, Faculty of Medicine-Zagazig University, Egypt

<sup>2</sup>Department of Medical Microbiology and Immunology, Faculty of Medicine, Zagazig University, Egypt

Corresponding author: Mahmoud Mostafa Diab, Email: [mahmouddiab63@yahoo.com](mailto:mahmouddiab63@yahoo.com)

## Abstract

**Background:** Allergic rhinitis (AR) is one of the most globally common diseases and usually persists throughout life. First-line drugs can be successfully used to control AR. However, once these medications are terminated, the majority of AR patients will reappear the symptoms of AR within a brief period. Thus, these medications do not appear to exert a long-term effect on the baseline Total Nasal Symptom Score. **To study the relationship between the gut microbiota types and allergic rhinitis. Patients and Methods:** This case control study was carried out on 52 school-aged patients presented at Oto-rhino-laryngology, Head and Neck (ORL-HNS) Department and Microbiology and Immunology department at Zagazig University. The patients were classified into 2 groups: Allergic rhinitis group: 26 individuals with allergic rhinitis Control group: 26 individuals without allergic rhinitis. All patients in this study were subjected to the personal history taking, physical examination and laboratory investigations including: eosinophilic count, skin prick tests (SPT) for common perennial and seasonal allergens, measurement of (total Ig E) and identifying bacteria (lactobacillus and bacteroides) by SYBR Green real time PCR. **Results:** Age was distributed as  $11.19 \pm 3.26$  and  $11.65 \pm 3.24$  respectively between case and control with no significant difference between groups. Mean disease duration was  $6.15 \pm 2.01$ , the majority were Intermittent and mild regard classification also the majority were trigger by inhalation. Skin prick test among cases group showed majority were house dust and date palm pollens. Absolute eosinophils counting was significantly higher among cases compared to control one. Cases were significantly higher regard IgE distribution. Lactic acid bacteria RNA was significantly higher among control group compared to cases group while Bacteroid bacteria RNA was significantly higher among cases group compared to control group. **Conclusion:** Lactic acid bacteria in gut microbiota of school-aged individuals may influence sensitization to different allergens.

**Keywords:** Allergic Rhinitis; Gut Microbiota; SYBR PCR; Ig E; Skin prick test

## INTRODUCTION

Allergic rhinitis is characterized by nasal congestion, rhinorrhea, sneezing, itching of the nose, and/or postnasal drainage. Additionally, airway hypersensitivity may

develop a decrease of the sense of smell and an inability to taste. Moreover, some patients experience sleep disturbances, decreased emotional wellbeing and social functioning, may be headache, and irritability (1).

Although the onset of allergic rhinitis may occur at any age, it is most common in children and at adolescence. The prevalence varies with age, less commonly occurring below 2 years of age. 2-6 years, (3.7%), 7- 12 years (9.3%), 13-19 years (9.1%), 20-29 years (14.3%), 30-39 years (10.2%), 40-49 years (7.6%), 50-59 years (8.6%), 60-69 years (4.8%) and over 70 years (1.8%)(2). In Egypt to assess the severity of allergic diseases in different Egyptian areas, it was concluded that prevalence of allergic rhinitis is 12.33% among school children from 11 to 14 years old (3).

A new international classification of allergic rhinitis has been proposed. Previously, allergic rhinitis was described as seasonal, perennial, or occupational. The new classification is based on the frequency and duration of symptoms (intermittent or persistent), and the severity of symptoms and effect on quality of life (mild or moderate- severe). People are then grouped according to a combination of the severity, frequency and duration of their symptoms (4).

The main role of allergy testing is to direct allergen avoidance and enable allergen identification if desensitization is being carried out. Specialist investigation may include skin-prick testing for reaction to a specific allergen or the measurement of allergen-specific immunoglobulin-E in a serum (Radioallergosorbent Test "RAST") in some individuals. A positive result does not necessarily mean that the allergen is causing clinical disease, and the results should be interpreted cautiously in the light of the clinical history (5)

The micro-organisms colonizing the gut perform different functions vital for human health, including processing of dietary constituents, regulation of host metabolism, immune system maturation, and development of oral tolerance. To date, numerous metabolic and immune disorders have been associated with gut microbiota dysbiosis in childhood, including inflammatory bowel disease, celiac disease, obesity, allergy, asthma and allergic rhinitis (6).

Epidemiologic evidence supporting a concept that children with greater microbial exposure in early life, through farming environments, pets, older siblings, and daycare settings, have a lower risk of developing asthma, rhinoconjunctivitis, atopic dermatitis and allergic rhinitis (7,8).

Therefore, the present study aimed to assess the relationship between the gut microbiota types and allergic rhinitis.

## **PATIENTS AND METHODS**

A case control study was carried out on 52 school-aged patients with allergic rhinitis presented at Oto-rhino-laryngology, Head and Neck (ORL-HNS) Department and Microbiology and Immunology department at Zagazig University.

Written consent obtained from all patients parents or their relatives before getting them involved in the study. Patients informed about any abnormal results of procedures and tests performed and were instructed and treated accordingly.

**Inclusion criteria:**

Patients presented with persistent or perennial type of allergic rhinitis, in which signs are present: (more than four days a week and for more than four consecutive weeks). Their age ranged from (6-18) years old. Patients were selected according to the ARIA classification (Allergic Rhinitis and its impact on Asthma), with two or more of the following allergic rhinitis symptoms: (Sneezing, aqueous rhinorrhea especially paroxysmal, nasal obstruction nasal itching – conjunctivitis "itching-lacrimation or redness).

**exclusion criteria:**

Patients with purulent rhinorrhea, pregnant and lactating women, diabetic patients, BMI values  $>30 \text{ kg/m}^2$ , patients presented with dyslipidemia (ldl cholesterol  $\geq 189 \text{ mg/dl}$  and/or triglycerides  $\geq 350 \text{ mg/dl}$ ), patients with systolic blood pressure  $\geq 160 \text{ mmhg}$  and/or diastolic blood pressure  $\geq 100 \text{ mmhg}$ , patients receiving treatment with antibiotics 30 days before the start of the study, patients receiving treatment with corticosteroids 30 days before the start of the study.

**Technical design:**

This study was done between June 2020 and December 2020. The patients were classified into: Allergic rhinitis group: 26 individuals with allergic rhinitis. They were 12 males and 14 females. The mean of their ages was  $11.19 \pm 3.26$  years. Control group: 26 individuals without allergic rhinitis in ORL-HNS Department, Zagazig University. They were 14 males and 12 females. The mean of their ages was  $11.65 \pm 3.24$  years.

Full history, clinical examination and laboratory examination including : Eosinophilic count by blood cell counter (Sysmex) and Skin prick tests (SPT) for common perennial and seasonal allergens were performed for all patients to confirm or exclude allergic rhinitis in patients and control. Total IgE (A0141) was measured by ELISA kit. Stool feces were collected from each patient in a storage container to identify bacteria (lactobacillus and bacteroides). Identifying bacteria (lactobacillus and bacteroides) by SYBR Green real time PCR.

**Statistical Analysis**

Data analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0). Qualitative data represent as number and percentage, quantitative continues group represent by mean  $\pm$  SD, the following tests were used to test differences for significance. Difference and association of qualitative variable by Chi square test ( $\chi^2$ ). Differences between quantitative independent groups by t test or Mann Whitney, correlation by Pearson's

correlation. P value was set at <0.05 for significant results & <0.001 for high significant result.

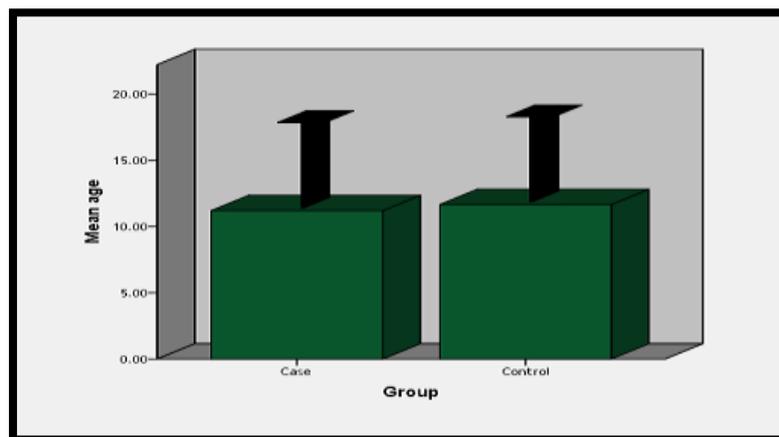
### Results:

The attainable results showed age was distributed as  $11.19 \pm 3.26$  and  $11.65 \pm 3.24$  respectively between case and control with no significant difference between groups (**Figure 1**).

Mean disease duration was  $6.15 \pm 2.01$ , the majority were Intermittent and mild regard classification also the majority were trigger by inhalation (**Table 1**). Regarding Skin prick test among cases group, majority were house dust and date palm pollens (**Table 2**).

Absolute eosinophils was significantly higher among cases compared to control one (**Figure 2**). Cases were significantly higher regard IgE distribution (**Figure 3**).

Concerning Fold change of Lactic acid bacteria and Bacteroides bacteria between cases and control groups, lactic acid bacteria RNA was significantly higher among control group compared to cases group while Bacteroid bacteria RNA was significantly higher among cases group compared to control group (**Table 3**).



**Figure (1): Age distribution between studied groups.**

**Table (2): Clinical characteristics among cases group:**

Variable		Cases (n=26)	
Duration (years)	Mean± SD	6.27±2.43	
	Median (Range)	6.5 (2-10)	
Variable		N	%
Allergic rhinitis	Intermittent	18	69.2
	Persistent	8	30.8
Allergic rhinitis	Mild	16	61.5
	Moderate to sever	10	38.5
Triggers	Inhalation	13	50.0

<b>Food</b>	<b>5</b>	<b>19.2</b>
<b>Both</b>	<b>8</b>	<b>30.8</b>

Table (3): Skin prick test among cases group:

Skin prick test	Cases (n=26)	
	N	%
House dust and Cotton	1	3.8
House dust and Date palm pollens	15	57.7
House dust and Wool	2	7.7
House dust	8	30.8

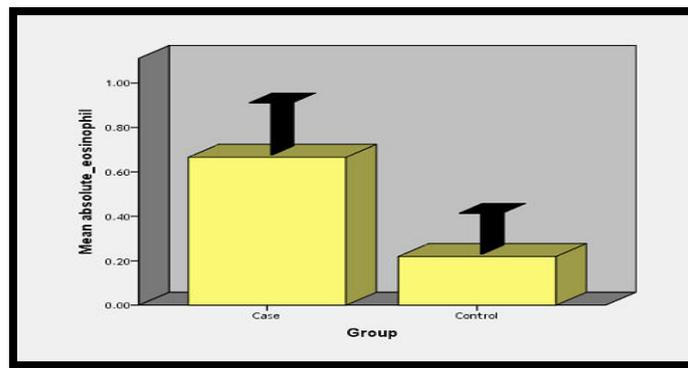


Figure (2): Absolute eosinophil comparison between cases and control

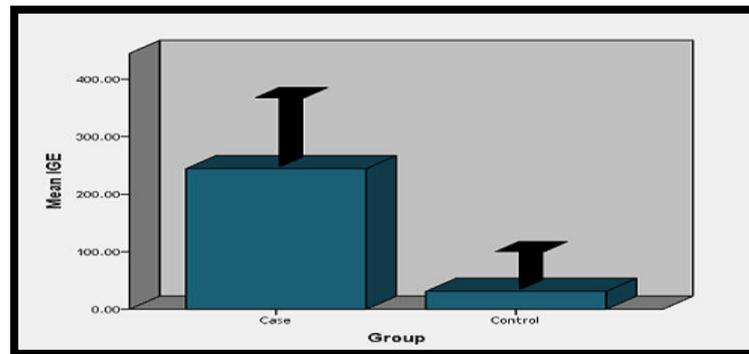


Figure (3): IgE distribution between groups.

Table (3): Comparison of Fold change of Lactic acid bacteria and Bacteroides bacteria between cases and control groups:

Variable	Case (n=26)	Control (n=26)	Test	P
Lactic acid RNA	0.21±0.10	0.98±0.06	MW 33.53	<0.001 **
Bacteroid RNA	11.07±1.84	0.95±0.08	t 28.05	<0.001 **

Sd: Standard Deviation, Mw: Mann Whitney Test, T: Independent T Test \*\*: Highly Significant (P<0.001)

## DISCUSSION

Allergic rhinitis (AR) is one of the most globally common diseases and usually persists throughout life. AR is defined as immunoglobulin E (IgE)-mediated non-infective inflammatory disease of the nasal mucosa after allergen exposure and a variety of immune active cells and cytokines are involved (5). Considering the unsatisfactory results of long-term AR treatment, a better understanding of relationship between gut microbiota and AR disease, and the further potential regulation mechanism of gut microbiota for AR is necessary (6).

Therefore, the role of probiotics in nutritional interventions have been investigated regarding to their beneficial effects on AR in improving patients' quality of life and reducing medication use. The beneficial roles of probiotics in allergic diseases have been investigated with increasing interest in animal models and human clinical trials, which indicate their significant influence on the gut microbiota composition and host immune system restoration (8).

Hence, the present study aimed to assess the relationship between the gut microbiota types and allergic rhinitis.

Our study revealed overall rate of sensitization to any allergen was 100% and majority of allergens were house dust and date palm pollens. There was significant difference between the studied groups regarding total IgE. The mean total IgE in patients group was 244 IU/ml. This came in agreement with **Wafaa et al. (9)**, **Chiu et al. (10)** who found the same results.

Also, **Saleem et al. (11)** found that the mean total IgE was 213 IU/ml. This finding is also similar to other reports that pointed to elevated serum level of IgE in patients with allergic diseases (12,13).

A significant relation has been demonstrated in studies between the levels of specific serum IgE and the probability of clinical rhinitis (14,15). However, any individual, atopic or not could show a demonstrable total IgE level. Parasitic infestation is a well-known cause of elevated IgE levels, which is needed to be ruled out, smoking also can enhance IgE production (16,17).

**Azad et al. (18)** conducted a Canadian Healthy Infant Longitudinal Development (CHILD) general population cohort study, using next-generation Illumina sequencing to profile the gut microbiota of 166 infants, identified a higher ratio of Enterobacteriaceae to Bacteroidaceae at 3 months of age to be predictive of food sensitization at 1 year.

**Arrieta et al. (19)** found that the ratio of Enterobacteriaceae to Bacteroidaceae could be a marker of gut microbiota immaturity because Bacteroidaceae tend to become more dominant with age. Importantly, these associations were still evident in analyses excluding infants with major microbiota-disrupting exposures (cesarean delivery, antibiotics, or formula feeding). A nested case control study examining the gut microbiota of 319 infants enrolled in the same CHILD cohort found that children

with a high risk of asthma at school age (classified as those with atopy and wheeze at 1 year) exhibited transient gut microbial dysbiosis during the first 100 days of life. The relative abundances of *Lachnospira*, *Veillonella*, *Rothia*, and *Faecalibacterium* species were significantly decreased in children with atopy.

**West et al. (20)** demonstrated deficiency in Bacteroidetes in pregnant mothers of infants with IgE-associated eczema, although this deficiency was not confirmed in infant microbiota. This study of 20 mother-infant dyads further showed a depletion of Ruminococcaceae in infants developing IgE-associated eczema and demonstrated correlations between specific microbial taxa and inflammatory cytokine responses.

Several prospective studies have found decreased microbial diversity to precede the development of eczema, atopic sensitization and allergic rhinitis, and asthma (21,22,23).

## CONCLUSION

Lactic acid bacteria in gut microbiota of school-aged individuals may influence sensitization to different allergens.

**No conflict of interest.**

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